REMARKS

Claims 60-69 are pending in the captioned application. Claims 60, 66, 68, 81, 90, 92, 93, 95, and 96 have been amended. This amendment does not introduce new matter. The amendments to claims 60, 66, 68, 81, 90, 92, 93, 95, and 96 are supported in the specification at page 4, lines 3-5.

Applicant respectfully requests that the amendments and remarks made herein be entered into the record of the instant application.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 60-96 under 35 U.S.C. § 112, second paragraph as indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner has rejected claims 60, 66, 68, 81, 90, 92-93 and 95-96 as indefinite because it is allegedly not clear from the recitation of "promoter...expression in a plant operably linked to," whether the plant or the promoter is operably linked to the subsequently recited claim elements. Applicant has amended claims 60, 66, 68, 81, 90, 92-93 and 95-96 to recite ", said promoter being" before "operably," in accordance with the Examiner's suggestion. This amendment is intended to clarify, not change the scope of, the claims.

Applicant believes the amendments to the claims overcome the rejection and respectfully request the Examiner's withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection Under 35 U.S.C. § 112, First Paragraph For Lack of Written Description

The Examiner has rejected claims 68-96 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, the Examiner contends that no guidance has been provided for the isolation or characterization of pyruvate kinase, acid invertase, starch synthase, 6-phosphofructokinase, sucrose synthase, and sucrose phosphate synthetase from any source, for the isolation and characterization of their corresponding genes, or for plant transformation

with such genes.

To fulfill the written description requirement of Section 112, it is well settled that the invention must be described in such detail that one skilled in the art would conclude that the inventor was in possession of the invention. *Regents of Univ. Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). There is no particular form that the written description must take. The written description can be satisfied by disclosure in the specification or the drawings. *Vas-Cath*, 935 F.2d, 19 U.S.P.Q.2d 1111 at 1559-1560. In addition, the written description inquiry turns on the knowledge of one of skill in the art:

> Since its inception, the Court of Appeals for the Federal Circuit has frequently addressed the "written description" requirement of § 112. A fairly uniform standard for determining compliance with the "written description" requirement has been maintained throughout: "Although [the applicant] does not have to describe exactly the subject matter claimed,... the description must clearly allow person of ordinary skill in the art to recognize that [he or she] invented what is claimed. *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989) (citations omitted; footnote omitted).

Vas-Cath, 935 F.2d at 1562-1563.

The Court of Appeals for the Federal Circuit has repeatedly considered the written description requirement and consistently found that exacting detail is not necessary to meet the requirement. *Martin v. Mayer*, 823 F. 2d 500, 3 U.S.P.Q.2d 1333 (Fed. Cir. 1987).

> "It is not required that the application describe the claim limitations in greater detail than the invention warrants. The description must be sufficiently clear that persons of skill in the art will recognize that the applicant made the invention having those limitations." *Id.*

As further support that the matter is well settled, one can look to more recent decisions. *In re Alton*, 76 F.3d 1168, 37 U.S.P.Q.2d 1578 (Fed. Cir. 1996).

> "If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if [not] every nuance of the claims is explicitly described in the specification, the adequate written description requirement is met." *Id.*

Applicant asserts that the written description requirement has been meet. In

accordance with case law, it is not necessary to describe the enzymes in exacting detail, particularly since the enzymes and encoding sequences had been isolated and were known and described in exacting detail in the art at the time of filing.

The specification as filed discloses Enzyme Commission (EC) numbers for pyruvate kinase, acid invertase, starch synthase, sucrose synthase, 6-phosphofructokinase (pyrophosphate) and sucrose phosphate synthetase. Given the EC numbers, one skilled in the art would understand that the specific enzymes had been isolated and characterized, see page 5, second paragraph of the specification. Each numeral in the EC number further specifies the characteristics of an enzyme. The EC numbers are not simply "naming a type of material generally known to exist," *University of California v. Eli Lilly and Co.*, 199 F.3d 1559, 1559, 1568; 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). The numbers are not general, but specific references to the function and structure of the particular enzymes. Moreover, the EC numbers could easily be used to locate the available purified enzymes and sequences encoding the enzymes. Thus, the enzymes were readily available to those skilled in the art at the time the application was filed in the U.S. Patent and Trademark Office, as evident by the EC numbers recited in the specification. This is in stark contrast to the situation in the Eli Lilly case where the patentee had claimed a genus of sequences with a particular function while disclosing only <u>one</u> sequence and other sequences in the genus were not known in the art.

Nucleic acid sequences encoding most of the enzymes from at least one organism and the corresponding amino acid sequences were known in the art at the time the application was filed. Amino acid and nucleic acid sequences encoding pyruvate kinase (EC 2.7.1.40) had been isolated and were known in the art at the time of filing (Inoue et al., 1986 (mammal cDNA and amino acid sequence), IDS Ref No.: C08; Ohara et al., 1989 (bacteria genomic DNA sequence), IDS Ref No.: C12; Burke et al., 1983 (fungi genomic DNA sequence), IDS Ref No.: C02; Blakeley et al., 1990 (plant cDNA sequence), IDS Ref No.: C01). Nucleic acids encoding acid invertase (EC 3.2.1.26) had been isolated and their sequences were known in the art at the time of filing (Taussig et al., 1983 (yeast DNA sequence), IDS Ref No.: C16; Martin et al., 1987 (bacteria DNA sequence), IDS Ref No.: C10). Both amino acids and nucleic acids encoding starch synthase (EC 2.4.1.21) had been isolated and their sequences were known in the art at the time of filing (Rohde et al., 1988 (plant sequence), IDS Ref No.: C14). Both amino acids and nucleic acids encoding sucrose synthase (EC 2.4.1.13)) had been isolated and their sequences were known in the art at the

time of filing (Salanoubat et al., 1987 (plant cDNA sequence), IDS Ref No.: C15).

For those enzymes that had been purified and characterized but for which nucleic acid sequences were not available in the art, from the purified proteins, the amino acid sequences could have been ascertained, following which cDNA clones for the respective genes could have been obtained or a respective antibody could have been used to screen an expression library of cDNA clones. This would have been well within the capability of a person skilled in the art in 1989. One skilled in the art could easily have isolated, used amino acid sequence information, or antibodies against the protein to clone genes encoding sucrose phosphate synthetase (EC 2.4.1.14) protein which had been isolated (Harbron et al., 1981, IDS Ref No.: C07; Walker et al., 1989, IDS Ref No.: C17) and 6-phosphofructokinase (EC 2.7.1.90) protein which had also been isolated (Kruger et al., 1987, IDS Ref No.: C09). Given the readily available proteins and encoding sequences, one skilled in the art at the time of filing could have readily obtained a precise characterization of all of the above enzymes and their coding sequences and would clearly have been able to visualize or recognize such enzymes and sequences from any source given the description in the specification and the state of the art.

Applicant respectfully disagrees with the Examiner's contention that the specification lacks written description support for plant transformation with genes encoding the above enzymes. The Examiner's attention is invited to page 8, line 17 through page 11, line 20 of the specification. Therein, methods of plant transformation, e.g. *in vitro* plant cell *Agrobacterium* mediated transformation, are disclosed. One skilled in the art would recognize that such transformation techniques are applicable to transforming most plant species. The disclosure of plant transformation techniques combined with the disclosure of the EC numbers of glycolytic enzymes, and the example of PFK transformed plants disclosed in the specification, in Example 1 at pages 12 and 13, provides adequate written description support for transgenic plants expressing one or more of the glycolytic enzymes disclosed in the specification.

In accordance with the Written Description Guidelines, the disclosure of a single species may provide an adequate written description of a genus when the species disclosed is representative of the genus. In the present instance, the glycolytic enzymes of the specification exhibit the common attribute of affecting levels of pathway intermediates. The EC numbers are indicative of the structure of the glycolytic enzymes, and the known role of each enzyme in steps in the pathway is outlined in Figure 1 of the specification. Thus,

plants transformed to alter expression of such enzymes also have the common attribute of affecting levels of pathway intermediates. The species disclosed in the specification, i.e., a plant transformed with PFK, is representative of the genus of plants transformed with a glycolytic enzyme because the transgenic plants disclosed exhibit altered amounts of intermediates which is the attribute that is representative of the genus of transgenic plants transformed with glycolytic enzymes.

The above reasoning supports the assertion the Applicant was in possession of the necessary common attributes of the elements possessed by the members of the genus of plants transformed with glycolytic enzymes. Thus, one skilled in the art would understand that the Applicant had possession of plants transformed with glycolytic enzymes that exhibit altered amounts of starch and/or sugar pathway intermediates.

In view of the forgoing reasoning, applicant respectfully submits that the rejection is in error and request withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejection Under 35 U.S.C. § 112, First Paragraph For Lack of Enablement

Rejection of claims 62, 77, and 95.

The Examiner has rejected claims 62, 77, and 95 under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably provide enablement for any tuber from any plant species, and therefore the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). In fact, well known subject matter is preferably omitted. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384; 231 U.S.P.Q.2d 81 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well know in the art."). Further, one skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. See *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941; 15 U.S.P.Q.2d 1321 (Fed. Cir. 1990) ("A decision on the issue of enablement requires determination of

whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention." *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278, 1291; 6 U.S.P.Q.2d 1065 (D. Del. 1991); see also *DeGeorge v. Bernier*, 768 F.2d 1318, 1323; 226 U.S.P.Q.758 (Fed. Cir. 1985). As the cases make clear, only when there is undue experimentation is Section 112 not met. Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been explained in *In re Wands* (8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988)), among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *Id.*

The Examiner contends that it would require undue experimentation on the part of one skilled in the art to produce tubers on a multitude of non-exemplified plants such as grasses and pine. Applicant respectfully disagrees with the Examiner and submits that the teaching of the present application clearly enables one skilled in the art to make and use the presently claimed invention. Applicant submits that one skilled in the art would understand that to make a transgenic tuber, one would begin with a species that produced tubers. Applicant further respectfully points out that no reasoning has been put forth in support of the notion that the claimed process would not work to generate transgenic tubers from other plant species that have tubers. Moreover, as taught in the specification, numerous promoters, including 35s CMV, nopaline synthase, octopine synthase, and patatin can be used to drive expression, see page 4, lines 16-22. The expression patterns of these promoters can encompass tubers. The specification teaches that constitutive promoters such as the 35s promoter are suitable for use in the invention, see page 4, second paragraph. One skilled in the art would have understood that the 35s promoter drives constitutive expression in a multitude of plant species. One skilled in the art would understand that using a promoter that drives constitutive expression, would result in expression that encompasses tubers. Thus, the skilled artisan could readily make transgenic tubers in plants given the teachings of the specification.

In addition, it is clear from the specification as filed that Applicant's invention encompasses any tuber, "particularly potato tubers," see page 4, lines 19-21. Such language certainly does not limit the scope of the invention to potato tubers, but merely puts forth potato tubers as a preferred embodiment. As explained above, examples of promoters that could drive expression in tubers are taught in the specification, see page 4, lines 16-22. Transformation of plants with patatin promoter is demonstrated in Example 1, at page 12 and the effect of expression in tubers is described in Table 3, at page 17. Applicant has also demonstrated that the patatin promoter is inducible and can drive expression in other plant organs such as leaves, see page 18, Table 4. One skilled in the art would reasonably expect that the patatin promoter could drive expression, inducible or otherwise, in the tubers of other plant species. Moreover, one skilled in the art would easily be able to identify transgenic tubers from species other than potato that had successfully been transformed using GUS reporter gene and one of the promoters taught in the specification, see page 12, second paragraph, wherein GUS transformation constructs are demonstrated. Assays for measuring sucrose content were also routine in the art and could readily have been applied to identify transgenic tubers generated by the claimed process of the invention. Given the routine amount of effort involved, the guidance provided by the specification, the presence of working examples, and the well known expression patterns of the promoters disclosed in the specification, one skilled in the art could easily make and use a transgenic tuber, using the process disclosed in the specification without resorting to undue experimentation. Thus, Applicant respectfully requests that the rejection be withdrawn.

Rejection of claims 68-96.

The Examiner has rejected claims 68-96 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. In particular, the Examiner contends undue experimentation would be required by one of skill in the art to identify and isolate the gene or genes which encode any other non-exemplified glycolytic enzyme, and to evaluate the effects of said gene(s) on a multitude of non-exemplified transformed plant cells and plants.

As argued above in response to the written description rejection, the glycolytic enzymes recited in the claims had all been isolated and characterized from a variety of origins by the time of filing. One skilled in the art could easily have identified and isolated the gene

or genes which encode any of the other glycolytic enzymes disclosed in the specification using techniques that were routine in the art or by reviewing publications in the art.

With respect to evaluating the effects of the recited genes on a multitude of non-exemplified transformed plant cells and plants, Applicant asserts that one skilled in the art could make and use the process disclosed in the specification to make the claimed transgenic plants of the invention. One skilled in the art, using only routine experimentation, could need only follow the steps disclosed in the specification for transforming a plant with a chimeric gene comprising PFK, and replace the PFK encoding nucleic acid with that encoding one of the other known glycolytic enzymes, the EC numbers for which are recited in the specification. To exemplify how one skilled in the art could make and use the claimed invention with enzymes other than PFK following the teachings of the specification, Applicant submits herewith as Exhibit A the Declaration Under Rule 37 C.F.R. § 1.132 of Dr. Stephen Andrew Coates, hereafter the "Coates Declaration." The Coates Declaration discloses four experiments that demonstrate potato plants transformed with a chimeric gene. In the first experiment, described in paragraph 8 of the Coates Declaration, the chimeric gene comprised an antisense nucleic acid sequence, complimentary to a nucleic acid coding sequence of invertase, operably linked to the patatin promoter[2]. In the second experiment, described in paragraphs 9 and 10 of the Coates Declaration, the chimeric gene comprised an antisense nucleic acid sequence, complimentary to a nucleic acid coding sequence of sucrose synthase, operably linked to the patatin promoter. Another group of plants were transformed with a chimeric gene that comprised a sense nucleic acid molecule encoding sucrose synthase, operably linked to the patatin promoter. In the third experiment, described in paragraph 11 of the Coates Declaration, the chimeric gene comprised an antisense nucleic acid sequence, complimentary to a nucleic acid coding sequence of pyruvate kinase, operably linked to the patatin promoter. Another group of plants were transformed with a chimeric gene that comprised a sense nucleic acid molecule encoding pyruvate kinase, operably linked to the patatin promoter. In the forth experiment, described in paragraph 12 of the Coates Declaration, plants were transformed with two different chimeric genes, the first equivalent to the sense oriented pyruvate kinase chimeric gene described for the third experiment, and the second chimeric gene comprised a sense nucleic acid molecule encoding

[2] Although not strictly a chimeric gene comprising a coding sequence for the enzyme, the results are indicative of the effect of modifying the level of enzyme activity in a plant which directly relates to modifying the amount of a metabolic intermediate.

phosphofructokinase operably linked to the patatin promoter.

In two of the four experiments, transgenic plants comprising chimeric genes having invertase antisense sequences or sucrose synthase sense or antisense sequences were selected that exhibit modified amounts of one or more glycolytic intermediates, Coates Declaration paragraphs 8 and 9. In the remaining two experiments, transgenic plants comprising chimeric genes having pyruvate kinase sense or antisense sequences or pyruvate kinase and phosphofructokinase sense sequences combined were selected that exhibit altered enzyme activity, an indirect indication of modified amounts of one or more glycolytic intermediates, Coates Declaration paragraphs 11 and 12. The four experiments were conducted using methods taught in the specification. As with the working examples in the specification, sugar levels were examined and found to be significantly increased in plants transformed with constructs having invertase or sucrose synthase sequences, *Id* at paragraphs 8 and 9. One would expect that modifications of amounts of intermediates would also occur in plants transformed with nucleic acids encoding other glycolytic enzymes such as pyruvate kinase, starch synthase, pyrophosphate or sucrose phosphate synthase. In addition, in experiment 1, where phenotypic effects were observed in the invertase anti-sense transformed plants, no deleterious effects were observed, *Id* at paragraphs 8. In comparison to the control plants, the plants expressing the nucleic acid encoding antisense invertase or sucrose synthase sense or antisense sequences exhibited altered sucrose content. The results demonstrate that one skilled in the art can predictably generate the claimed transgenic plants by following the teachings and working examples of the specification.

With respect to starch synthase, the Examiner's attention is invited to the Declaration Under Rule 37 C.F.R. § 1.132 of Dr. Michael Meyrick Burrell, a copy of which is provided herewith as Exhibit B. The Declaration of Dr. Michael Meyrick Burrell, hereafter the "First Burrell Declaration" was submitted to the United States Patent and Trademark Office on August 19, 1996 in connection with the prosecution of U.S. Patent Application No. 08/192,493, which issued as U.S. Patent No. 5,830,724 on November 3, 1998. The First Burrell Declaration discloses the successful transformation of hybrid maize plants with a wheat homologue of the gene encoding starch synthase (in the sense orientation), see paragraph 4. Transgenic lines that exhibited altered starch quantities, particularly reduced amylose content, were selected, see paragraph 6. A modification in the amount or type of starch is an indirect measurement of modification in the amount of limiting intermediates in the starch biosynthesis/degradation pathways. These results support enablement of the

present invention because they demonstrate that the methods of the invention can be used to generate a plant with modification of the amount of a metabolic intermediate.

With respect to sucrose synthase and dual suppression of invertase and sucrose phosphate synthase, the Examiner's attention is invited to the Declaration Under Rule 37 C.F.R. § 1.132 of Dr. Michael Meyrick Burrell, executed February 25, 1997, provided herewith, hereafter the "Second Burrell Declaration." Therein, transgenic potato plants were generated with a chimeric gene encoding sucrose synthase in the sense orientation. Plants were also generated with a chimeric gene encoding sucrose synthase in the antisense orientation, see paragraph 7. The sense and antisense transgenic plants were pooled and compared to control plants, Second Burrell Declaration at page 4 . The pooled transgenic lines showed significant difference in starch content in comparison to the control plants. A modification in the amount or type of starch is an indirect measurement of modification of in the amount of limiting intermediates in the starch biosynthesis/degradation pathways. These results combined with the results presented in the Coates Declaration support enablement of the invention with respect to plants transformed with chimeric genes encoding starch synthase. The remaining experimental results presented in the Second Burrell Declaration demonstrate that the methods taught in the specification can be used successfully to make a transgenic plant having more than one modified glycolytic enzyme. The transgenic plants generated comprised antisense invertase and antisense sucrose phosphate synthase constructs and exhibited modification in glucose, fructose, and sucrose amounts in comparison to control plants. These results support enablement of the present invention because they demonstrate that the methods of the invention can be used to generate a plant altered expression of a glycolytic enzyme that has modification of the amount of a metabolic intermediate.

Subsequent to the filing of the present application, others have employed the methods taught in the present application to obtain successfully and predictably plants transgenic for one of the recited glycolytic enzymes that exhibit a modification in the amount of an intermediate in glycolytic, starch, or sugar metabolic or degradation pathways. Transgenic tobacco plants with constitutive expression of the nucleic acid encoding pyruvate kinase have been produced and exhibited reduced levels of pyruvate kinase enzyme activity in leaves, and increased phophoenolpyruvate in the leaves (Gottlob-McHugh et al., 1992, IDS Ref No.: C05). Transgenic plants transformed to express 6-phosphofructokinase (pyrophosphate) exhibited more hexose phosphates and less 3-phosphoglyceric acid and

phosphoenolpyruvate (Hajirezaei et al., 1994, IDS Ref No.: C06). Plants transformed to express a nucleic acid encoding starch synthase in the antisense orientation exhibited significantly reduced starch content (U.S. Patent No. 5,365,016, IDS Ref No.: A01). The subsequent published results are consistent with the pathway scheme disclosed in Figure 1 of the specification, based in part on the discoveries of the Applicant, and achieve the results of the claimed process, i.e., modulation of the amount of a metabolic intermediate in a transgenic plant. The results also demonstrate that the claimed invention is not unpredictable and can be successfully made and used by one skilled in the art without undue experimentation.

Furthermore, the Examiner contends von Schaewen et al. (1990, EMBO, 9:3033-3044) hereafter "von Schaewen", demonstrates that the state of the art of transforming plants with genes encoding glycolytic enzymes is unpredictable. The results of von Schaewen with respect to tobacco transformed to express a fusion invertase protein demonstrate deleterious effects on plant health, and less appreciable, though notable, discoloration of leaves in transformed *Arabidopsis* plants.

Von Schaewen targeted a yeast invertase gene to cell walls in plants, which do not normally express the sucrose metabolizing enzyme, loading these plant cells with invertase enzyme where it is not typically found. Upon observing deleterious effects, one skilled in the art would clearly be able to avoid or reduce such expression, without resorting to undue experimentation, by targeting plant tissues or cells where expression is normally found. The specification provides an example of such targeting at page 12, second paragraph, where plants transformed with a chimeric gene comprising PFK operably linked to a tuber specific promoter are disclosed. As discussed above, other transgenic plants with modified levels of glycolytic enzyme do not exhibit deleterious phenotypic effects. Thus, it is not necessarily evidence of unpredicability.

Applicant has demonstrated through submission of the Coates Declaration, the First and Second Burrell Declarations, and subsequent publications in the art that undue experimentation would not be required by one skilled in the art to produce a transgenic plant that expresses a glycolytic enzyme and exhibits a modification of the amount of a metabolic intermediate. The results of the experiments presented in the Coates Declaration and the First and Second Burrell Declarations demonstrate that one skilled in the art can readily identify and isolate plants with modified amounts of metabolic intermediates and plants having characteristics related to modified amounts of metabolic intermediates.

The Examiner also contends that it is unclear whether plants transformed with more than one glycolytic gene would be adversely affected, given the "double dose" of glycolytic enzyme alteration. These enzymes, although chemically diverse, are all related in that they function in plant cells to modify the amount of metabolic intermediate in glycolysis or in a pathway for the synthesis or degradation of starch, sucrose, or a reducing sugar. Applicant asserts that one skilled in the art would expect a plant engineered to express two of the enzymes to exhibit a modification of the amount of a metabolic intermediate, since plants engineered to express individual glycolytic enzyme genes exhibit such characteristics. Since the role of the enzymes in the glycolytic pathway was understood at the time of filing, in light of the Applicant's discoveries, one skilled in the art would have been able to predict how expression of two enzymes would effect the amounts of the particular metabolic intermediates that correlate to the enzymatic reactions. The results presented in the Second Burrell Declaration and the Coates Declaration, both described above, corroborate this reasoning and demonstrate that plant cells transformed with two gylcolytic enzymes encoding chimeric genes have modified amounts of intermediates.

In view of the forgoing amendments and reasoning, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

CONCLUSION

Applicant respectfully requests that the above-made amendments and remarks be entered and made of record in the instant application. Withdrawal of the Examiner's rejections is earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone Margaret Brivanlou at (212) 790-6424 to discuss the same.

Respectfully submitted,

Date: July 14, 2003

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Enclosures